PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 501543/JEP	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/000719**	International Filing Date *(day/month/year)* 10 June 2003	Priority Date *(day/month/year)* 7 June 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] A61K 31/16, 31/445, 31/505, 35/36, 38/43, 47/10, 47/14, 31/40, A61P 35/00, 35/04

Applicant

SCOTT, Kieran Francis et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of **5** sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of the report
5 January 2004	21 September 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **M. Ong** Telephone No. (02) 6283 2491

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000719

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **6-11, 14-17**	**YES**
	Claims **1-5, 12-13**	**NO**
Inventive step (IS)	Claims **6-11, 14-17**	**YES**
	Claims **1-5, 12-13**	**NO**
Industrial applicability (IA)	Claims **1-17**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

Novelty (N): Claims 1-5 and 12-13

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1: WO 1998/005349
D2: US 5 942 402
D3: EP 1 300 159
D4: ATTIGA, FA et al.
D5: DE SOUZA, PL et al.
D6: WO 2003/0014082

The invention is directed to the inhibition, reduction or treatment of prostate cancer through the administration of a PLA_2 inhibitor, wherein the prostate cancer cells are androgen independent prostate cancer cells, and the PLA_2 can be $cPLA_2.\alpha$, $sPLA_2$ -IIA inhibitor or a conformationally constrained molecule derived from a peptide consisting of amino acid residues 70-74 of a human s PLA_2-IIA protein, or the equivalent residues in other $sPLA_2$ proteins. . The method of detecting prostate cancer or a metastases comprising the determination of PLA_2 mRNA or polypeptide expressed in a test sample, and comparing the level of the PLA_2 mRNA or polypeptide, with that of a normal or healthy individual is defined in claims 12 and 13. Claim 14, further defines a method of assessing the predisposition of a subject to prostate cancer by determining the presence of a polymorphism or an epigenetic change in a PLA_2 gene of the subject.

D1 teaches a method or diagnosing and treating cancers such as prostate cancer and benign prostate hyperplasia, by the binding and inhibition of PLA_2. This is carried out using PLA_2 antagonist like antibodies, small molecules or fragments that are related to the binding molecules of PLA_2 and an antisense construct etc. D1 discloses methods of detecting levels of PLA_2 protein, or PLA_2 mRNA in cells using common assay techniques, for example, ELISA, PT-PCR western blots etc.

D2 similarly, discloses a method for diagnosing , treating, and monitoring progression, remission or recurrence of abnormal cell growth, prostate cancer in particular, through the provision of PLA_2 inhibitors. Measurements of PLA_2 mRNA or polypeptides through the comparisons of test samples using conventional assay methods are also taught.

D3 teaches a composition for the prevention or treatment of cancer, including prostate cancer comprising type-X $sPLA_2$ inhibitor. D4 discloses that treatment of DU-145 and PC-3 prostate tumour cells, with PLA_2 inhibitor, 4-bromophenacyl bromide, inhibited cell invasiveness of both cell lines. Treatment of DU-145 with quinacrine, another PLA_2 inhibitor, similarly inhibited cell invasion through Matrigel. D5 discloses quinacrine as an inhibitor of phospholipase A_2 action that is used with paclitaxel against prostate cancer cells.

Claims 1-5, 12 and 13 are not considered to be novel, in view of the disclosures of the prior art cited above.

D6 was published after the priority date and will not be considered further. See however the indication in Box VI.

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
P, X WO 03/014082	20 February 2003	29 July 2002	9 August 2001

This document teaches the essential features of claims 1-5, in that it discloses $sPLA_2$ inhibitors for use in prostate cancer treatment. With regard to the document(s) listed in Box VI under "certain documents cited", these are documents published prior to the international filing date but later than the priority date claimed but which would otherwise be considered to be of particular relevance.

Under the PCT, novelty is considered only in respect of documents published before the priority date. The relevance of a document published after the priority date is dependent upon national law. Such documents are excluded from consideration in preliminary examination, under the PCT Guidelines but have been included here for information.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

Inventive Step (IS): Claims 1-5, 12 and 13

As novelty above.

The subject matter of claims 6-11 and 14-17 is not obvious and meets the requirements of Article 33(33) PCT with regard to the requirements for inventive step.

Industrial Applicability (IA): Claims 1-17

Claims 1-17 have industrial applicability